REMARKS

Applicant has carefully considered the points raised in the Office Action and believes that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Status of the claims

Claims 6, 9, 11-13, 16-18, 21, 23, 25, 27-35, 37, 39, 41, and 43-50 are pending. Claims 16-18, 21, 23, 25, and 27-33 were previously withdrawn from consideration as drawn to a non-elected invention. Claims 1-5, 7-8, 10, 14-15, 19-20, 22, 24, 26, 36, 38, 40, and 42 were previously canceled. By virtue of this response, claims 6 and 50 have been amended. Therefore, claims 6, 9, 11-13, 34-35, 37, 39, 41, and 43-50 are currently under examination.

The amendments to the claims are supported by the specification for example on page 24, line 22 and on page 36, lines 9-13. No new matter has been added by the foregoing amendments.

With respect to any claim amendments or cancellations, Applicant has not dedicated to the public or abandoned any unclaimed subject matter and moreover has not acquiesced to any rejections and/or objections made by the Patent Office. Applicant expressly reserves the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Rejoinder of claims

Applicants acknowledge with appreciation the rejoinder of claims 35, 37, 43, and 44 with Group I, which was elected with traverse in Paper No. 33.

Notice to comply with sequence disclosure requirements

The Office Action states that Figures 2, 11, and 12 must be amended to include SEQ ID NOs corresponding to each disclosed amino acid sequence, in compliance with the sequence disclosure requirements. In a telephone conversation between Applicant's representative and the Examiner on June 13, 2003, the Examiner stated that there is no requirement to add sequence identification numbers to the figures so long as the sequences that are represented in the claims are identified in the figure legends. Applicant notes that the figure legends were previously amended to include sequence identification numbers in paper no. 28. Therefore, Applicant respectfully submits that the application is in compliance with the sequence disclosure requirements and requests that the requirement to comply be withdrawn.

Rejection under 35 U.S.C. § 101

Claims 6, 9, 11-13, 34, 35, 37, 39, and 41-44 are rejected under 35 U.S.C. § 101 as allegedly directed to non-statutory subject matter because the claimed compound allegedly reads on naturally-occurring materials. Applicant respectfully notes that the claim limitation "wherein cysteines 173 and 176 are absent or blocked" removes the claimed compound from the ambit of naturally-occurring materials. However, in accordance with the Examiner's recommendation and solely to expedite prosecution, Applicant has amended claim 6 to recite the term "isolated," thereby obviating the rejection.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 101.

Rejection under 35 U.S.C. § 102(b)

Claims 6, 34, 35, 45-46, and 49 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Binz et al., FR 2 718 452 ("Binz").[1] Applicant respectfully traverses this rejection.

With respect to compound claims 6, 34, and 35, Binz does not disclose a compound that comprises a contiguous sequence of amino acids within the sequence representing residues 149-177 of the G protein of RSV, wherein cysteine residues 173 and 176 are absent or blocked, as recited in the claims as currently amended.

With respect to method claims 45-56 and 49, Binz does not teach a method of inhibiting the cytopathic effect of RSV. The disclosure in Binz is directed to polypeptides for use in the preparation of immunogens and the development of vaccines against RSV. There is no teaching in the Binz citation to show that any of the specific peptides exemplified therein are capable of inhibiting the infectivity of RSV. More specifically, there is nothing in this citation to suggest that the peptides are capable of inhibiting the cytopathic effect of RSV. In fact, Binz teaches away from a method of using RSV peptides to inhibit the cytopathic effect by the statement that "Applicant has demonstrated that the injection of such compositions affords protection, *not by a neutralizing effect*, but by a systemic immune response of the body." See U.S. Pat. No. 6,113, 911, col. 5, lines 29-31 (emphasis added), which claims priority to the cited reference. The results presented in Binz merely show that the disclosed peptides are capable of inducing an immune response against the G protein of RSV, and do not disclose use in a method of inhibiting the cytopathic effect of RSV as claimed.

In conclusion, Binz neither teaches a compound comprising a contiguous amino acid sequence within the sequence representing residues 149-177 of the G protein of RSV, with both

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[1] Applicant respectfully notes that Binz et al. published on October 13, 1995, so the rejection under 35 U.S.C. § 102(b) is improper, since this is less than one year prior to Applicant's priority date of June 5, 1996.

cysteine residues 173 and 176 absent or blocked, nor a method for using such a peptide to inhibit the cytopathic effect of RSV. Therefore, Binz does not anticipate the present invention.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b).

Rejection under 35 U.S.C. § 103(a)

Claims 6, 11-13, 34, 35, 37, 39, and 43-50 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Binz et al., FR 2 718 452 ("Binz") and Langedijk et al., *J. Gen. Virol.* (1996) 77:1249-1257 ("Langedijk"). Applicant respectfully traverses this rejection.

As discussed above, Binz does not teach a compound comprising a contiguous sequence of amino acids within the sequence representing residues 149-177 of the G protein of RSV, wherein cysteines 173 and 176 are absent or blocked, and does not teach a method of inhibiting the cytopathic effect of RSV, as presently claimed. Langedijk does not supply these missing claim elements, so the combination of Binz and Langedijk does not allow one of skill in the art to arrive at the claimed invention..

Langedijk discloses a peptide representing amino acid residues 158-189 of BRSV-G protein, but does not teach a peptide representing a contiguous sequence within residues 149-177 of the RSV G protein, and also does not teach such a peptide with cysteine residues 173 and 176 absent or blocked. Langedijk also does not teach a method for inhibiting the cytopathic effect of RSV. Further, Langedijk does not teach RSV G protein peptides with detectable markers as in claims 11-13, a peptide wherein one or more amino acids is replaced by its corresponding D-amino acid as in claim 37, or a compound comprising the amino acid sequence of SEQ ID NO:39 as in claims 43 or 44.

The Examiner states that Langedijk teaches that "the immunogenicity of the derived peptide possesses the same immunogenicity as the originals." As discussed above, Applicant is not claiming immunogenicity, but rather is claiming a method for inhibiting the cytopathic effect

of RSV in claims 45-49. Further, Langedijk does not teach immunogenicity of the disclosed peptides, as asserted by the Examiner. Rather, Langedijk teaches affinity of anti-RSV antibodies for the disclosed peptides *in vitro*. In any case, Langedijk does not teach or suggest a method for inhibiting the cytopathic effect of RSV by contacting an RSV susceptible cell with a compound of the present invention.

In conclusion, neither Binz nor Langedijk alone or in combination teaches or suggests the claimed compounds or a method of using them to inhibit the cytopathic effect of RSV. Therefore, the claimed invention is not unpatentable in view of these references.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

Rejection under 35 U.S.C. §112, first paragraph

Claims 9 and 41 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking adequate written description. Applicant respectfully traverses this rejection.

The Examiner asserts that there is not enough information in the literature concerning D-amino acid substitutions to guide a person skilled in this field to predict which amino acids should be replaced with a corresponding D-amino acid. Applicant maintains, however, that this methodology was standard in the art by the filing date of the present application. For example, the specification on page 8, lines 14-18, refers to a Choreo and Goodman, 1993, reference as a guide for preparation of retro-inverso amino acid sequences. This paper, which was incorporated into the specification by reference (see page 42, lines 31-33), provides adequate written description for the claimed invention.

The Examiner cites the *Eli Lilly* decision in support of this rejection. However, *Eli Lilly* is inapplicable to the presently claimed invention. The court in *Eli Lilly* found the written description inadequate because the Applicant disclosed how to arrive at the claimed invention but failed to provide the sequence of the claimed invention corresponding to a portion of the

recited claim. In contrast, in the present case, Applicant has disclosed the sequence of amino acids 149-177 of the RSV G protein and has claimed a compound comprising a sequence within this defined region. Since the sequence of the claimed compound has been disclosed, sufficient written description is provided to support the claimed invention. Further, it is well known that amino acids within this defined sequence may be substituted with D-amino acids to improve stability (see page 8, lines 28-31 of the specification).

Indeed, a common approach at the time of filing was to construct a series of peptides comprising the same sequence except for sequential replacement of an L-amino acid with its corresponding D-amino acid along the sequence. This approach is exemplified in Losardo et al. (1995) *Int. J. Peptide Protein Res.* 45:194-199, a copy of which is attached as Exhibit C. The results presented in this publication show that routine sequential substitution of L-amino acids for corresponding D-amino acids gave arise to peptides with increased *in vivo* stability. We submit that any competent researcher in this field would have been able to conduct similar substitutions on peptides derived from residues 149-177 of the RSV G protein without difficulty.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

Claims 6, 9, 11-13, 34, 35, 37, 39, 41, and 43-50 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled. Applicant respectfully traverses this rejection.

The Examiner states that the specification is enabling for using peptides 1-4 of Figure 12 to bind a HEp-2 cell infected with RSV and inhibit the cytopathic effect of the virus, but allegedly does not provide enablement for use of such a peptide in a method of therapy for treatment of a human RSV infection. Applicant respectfully traverses this rejection.

As an initial matter, claims 6, 9, 11-13, 34, 35, 37, 39, 41, 43-44, and 50 are all directed to *compounds*. Since the stated basis for the rejection is that the specification allegedly does not

provide enablement for a "method for using the peptide as a therapeutic composition to treat human RSV infection" (Office Action, page 6), these compound claims do not appear to be encompassed within the scope of this rejection, since they are not directed to methods of use. Applicant further notes that claims 45-49 are directed to *a method of inhibiting the cytopathic effect of RSV, which the Examiner has stated is enabled by the specification for peptides 1-4 of Figure 12*. (Office Action, page 6)

The Examiner asserts that the specification teaches that compounds of the invention inhibit RSV-induced cytopathic effect, but that "the scope of the invention read [sic] on use of any or all derivatives of the fragment of 149-197 for treating RSV infection in any situation." Office Action, paragraph 18. Applicant strongly traverses this statement. The claims are limited to those polypeptides within a defined amino acid sequence and include structural limitations with regard to disulfide formation and glycosylation, as well as the functional limitation that the compounds must have the ability to inhibit infectivity of RSV, and thus do not read on "any or all derivatives."

The Examiner states that it would require undue experimentation to make and use the claimed invention based on the disclosure in the specification. In support of this assertion, the Examiner states that mutation of RSV infection is very frequent and unpredictable. The Examiner asserts that this unpredictability is manifested by (1) the nature of the antigenicity of RSV; (2) the fact that the RSV G protein has a high degree of strain to strain diversity and stereotype specificity; (3) RSV elicits an imperfect immune response; and (4) enhanced disease in children is suspected to be caused by administration of an RSV vaccine. Office Action, paragraph 19. Applicant respectfully maintains that none of these arguments are relevant to a discussion of enablement of the claimed compounds or methods of inhibiting the cytopathic effect of RSV.

The Examiner has based the rejection on use of the compounds of the invention in a vaccination strategy, which is not what is presently claimed. A person skilled in the relevant

field would understand that methods that protect against viral infectivity by inhibiting the virus-induced cytopathic effect, as claimed, are completely different than methods that involve immunization or vaccination strategies. The claimed methods involve inhibiting the cytopathic effect of RSV by *contacting an RSV susceptible cell* with a compound of the invention, *not inducing an immune response by vaccination*. Further, the Examiner's concerns about lack of predictability are not well-founded since the claimed region of amino acids 149-177 of the G protein of RSV is surprisingly well conserved within human isolates of RSV and also across species, as discussed in the specification.

Attached as Exhibit A is a declaration under 37 C.F.R. §1.132 by Dr. Joseph Varghese, attesting to the fact that a person skilled in the art would be able to readily design and test compounds other than those exemplified in the present specification in order to obtain antiviral agents capable of inhibiting the cytopathic effect of RSV as claimed, based on the disclosure in the specification. Dr. Varghese states that a suitable assay for determining the impact of peptides on the cytopathic effect of RSV is described in the specification on page 36, line 32 to page 37, line 9, and that other suitable alternative assays were well known to those skilled in the field as of the priority date of June, 1996. Dr. Varghese further states that the application clearly defines the region of the RSV G protein that is capable of inhibiting the cytopathic effect and that given that suitable screens were available prior to the filing date, a skilled artisan would have been able to screen large numbers of candidate compounds without undue experimentation as of the filing date.

Dr. Varghese discusses a paper published by Applicant after the filing date of this application, which shows that peptides derived from the claimed region of the RSV G protein, other than those exemplified in the working examples of the application, are capable of inhibiting an RSV-induced cytopathic effect in human epithelial cells. A copy of this publication, Gorman et al. (2001) *J. Biol. Chem.* 276:38988-38994, is attached to this response as Exhibit B.

In summary, the specification teaches how to make the claimed compounds and how to use such compounds in a method for inhibiting the cytopathic effect of RSV, *which the Examiner states in paragraph 17 of the Office Action is enabled with respect to peptides 1-4 of Figure 12*. Further, Applicant submits a declaration herewith that attests to the fact that it would have been within the skill of the art at the time of filing to make and test other peptides within the scope of the claims, based on the disclosure in the specification. Applicant also submits a publication herewith that shows that a number of such peptides have been prepared that are capable of inhibiting the cytopathic effect of RSV as claimed.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 6, 35, 39, 41, 43, 45, 47, and 49-50 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite due to recitation of the term "comprising." The Examiner states that "comprising" is open language and therefore fails to define the precise structure of the claimed compound. Applicant respectfully traverses this rejection.

According to the MPEP, the standard for whether claims meet the requirement of definiteness under 35 U.S.C. § 112, second paragraph, is whether they "define the patentable subject matter with a *reasonable* degree of particularity and distinctness." MPEP § 1273.02, emphasis added. Definiteness of claim language must be analyzed, *inter alia*, in light of "the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made." *Id.*

Although "comprising" is open language as noted by the Examiner, the present claims also recite limitations that are clear and definite, and apprise one of skill in the art of the boundaries of the claimed invention. "Comprising" is a well-recognized term of art synonymous with "including," which permits other elements to be added to a claimed invention and still fall

within the scope of a claim. MPEP § 2111.03. Therefore, recitation of the term "comprising" does not render a claim indefinite. Rather, it allows *non-recited* elements to be added to what is recited in the claim. In the instant case, the claims define the invention by recitation of definite limitations, and the potential inclusion of additional non-recited elements does not render the claim indefinite.

The instantly-claimed invention requires a contiguous sequence of amino acids within a specified, recited polypeptide sequence, with the limitation that both cysteines are absent or blocked. The claims also include the limitations that the compound is not glycosylated and that the compound has the ability to inhibit infectivity of RSV. A compound including a contiguous amino acid sequence within the specified region of RSV G protein that has both cysteines absent or blocked, is unglycosylated, and is able to inhibit infectivity of RSV falls within the scope of the claims. Compounds that do not possess these limitations are not encompassed by the claims. Thus, the scope of the subject matter included within the claims is clear and definite. Any compound encompassed by the claims must possess the positive, clear limitations discussed above. As noted in MPEP § 2173.04, "[i]f the scope of the subject matter embraced by the claims is clear, and if applicants have not otherwise indicated that they intend the invention to be of a scope different from that defined in the claims, then the claims comply with 35 U.S.C. 112, second paragraph." With respect to the present claims, Applicants have defined the claimed invention with more than a reasonable degree of particularity, as set forth in MPEP § 1273.02, by inclusion of several limitations that define the scope of the invention.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Claims 45-49 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly incomplete due to omission of essential steps such as how to contact an infected cell, whether or

not the contact is made *in vitro* or *in vivo*, the dosage used, and length of treatment. Applicant respectfully traverses this rejection.

A similar rejection was made in paper no. 21 and was withdrawn in paper no. 26, since it was not reiterated. (See Paper no. 26, page 2, which states, "Please note any ground of rejection that has not been repeated is removed.") As discussed by Applicant in paper no. 24, there is no need to specify steps that are common to the art that are not required to distinguish the claimed invention from the prior art. As set forth in MPEP § 2172.01, to sustain a 35 U.S.C. § 112, second paragraph rejection, omitted steps must be "essential elements of the invention as defined by applicant(s) in the specification." With regard to the instantly-claimed invention, there is nothing in the specification to suggest that the steps mentioned by the Examiner are essential features of the claimed invention.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

CONCLUSION

Applicant has, by way of the amendments and remarks presented herein, removed the issues for the rejections and addressed all issues that were raised in the outstanding Office Action. Accordingly, reconsideration and allowance of the pending claims are respectfully requested. If it is determined that a telephone conversation would expedite the prosecution of the application, the Examiner is invited to telephone the undersigned at the number given below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. **273402004000**.

Respectfully submitted,

Dated: July 14, 2003

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